REMARKS

Support for new Claims 39-40 and 48 may be found as follows:

"A method of treating a diseased or injured invertebral disc (page 3, lines 8-9 ("A method for treating invertebral diseases ..."); page 3, lines 19-21 (treating various human intervertebral disc diseases and injuries such as idiopathic scoliosis, disc herniation, disc degeneration, and spinal stenosis); page 8, lines 6-12 (the method may be used to treat an area of the disc that is defective, e.g., damaged or degenerated; the human intervertebral disc cells obtained according to the present invention are used in treating disc diseases in human patients));

having nucleus and annulus regions (page 5, lines 13-14 (regions annulus and nucleus are visually identified"); page 11, lines 19-20 (Regions of annulus and nucleus were visually identified and representative pieces of annulus and nucleus were dissected.); page 11, line 31 ("Disc cells from both the annulus and nucleus grew well on the mesh lattice."));

obtaining live intervertebral disc cells (page 2, lines 29-30 ("an explant is first obtained from a human disc specimen"); page 4, line 31-page 5, line 1 ("disc tissue is surgically removed from a normal disc of a patient"));

said intervertebral disc cells are obtained from said human patient to be treated (page 3, line 11 ("healthy disc specimens are obtained from the patient to be treated"); page 4, lines 25-26); page 8,-lines 17-18 ("To this end, health disc specimens are obtained from the patient to be treated."));

culturing said intervertebral disc cells under conditions to propagate disc tissue (page 2, lines 25-27 ("cultured in vitro in the presence of a cell stimulant ... to form monolayer cultures"); page 3 lines 4-7 (cell culture media and cell stimulants may be added so that the cells further proliferate and re-express extra cellular materials); page 5, line 22-page 6, line 8; page 6, lines 10-29; page 6, lines 10-19 (carrier materials may include collagen)); and

implanting the cultured disc tissue into a target disc area needing treatment in a human patient (page 3, lines 9-10 ("implanting the cultured human intervertebral disc cells ...into the site to be treated"); page 3, lines 17-18 ("The implantation can be performed by conventional surgical methods known in the art."); page 5, line 5 ("inserted into site with disc degeneration in that same patient."); page 9, line 24-page 10, line 17 ("The implantation can be conducted by

standard transplantation techniques as will be clear to an ordinarily skilled artisan."); page 11, lines 3-9)).

Claim 41 requires that the "intervertebral disc cells are minced to obtain an explant prior to culturing." Support may be found at page 2, lines 29-30 ("an explant is first obtained from a human disc specimen"); page 5, line 16 ("The disc tissue to be cultured is minced into 1-2 mm square pieces . . .".).

Claims 42-43 and 49-50 require that the cultured intervertebral disc tissue be combined with a carrier material such as one selected from alginate, agarose, collagen, and derivatives and mixtures there of. Support may be found at page 3, lines 2-4; page 6, line 10-page 8, line 3; page 8, line 26-page 9, line 16. In addition, collagen is specifically used in Example III. (Page 14.)

Claims 44-45 and 51 require that the explant is cultured in the presence of serum, growth factors or cytokines and on such growth factors as transforming growth factor beta (TGF-ß). Support may be found at page 3, lines 4-8 ("Typically, cell culture media, and optionally, cell stimulants such as fetal bovine serum, growth factors and the like are added to the three-dimensional structure such that the cells further proliferate and re-express extracellular matrix materials."); page 5, lines 26-31.

Claim 46 requires that the implanting step "debride diseased or injured disc tissue" and then deliver the cultured disc cells into the area of debridement, e.g., the target area. Support may be found at page 10, lines 11-17.

Claim 47 requires that the cultured explant monolayer tissue be isolated and further propagated upon passaging; isolating the tissue from the monolayer and dispersing the isolated disc tissue in a carrier material to form a three-dimensional structure and culturing the three-dimensional structure.

Claim 52 is directed to a method for preparing a cultured intervertebral disc tissue comprising; obtaining live intervertebral disc tissue; culturing the disc tissue; and keeping the cultured disc tissue viable until use. Claim 53 is directed to the disc tissue for use in treating human disc diseases or injuries. Support for Claims 52-53 may be found as follows:

obtaining live intervertebral disc cells (page 2, lines 29-30 ("an explant is first obtained from a human disc specimen"); page 4, line 31-page 5, line 1 ("disc tissue is surgically removed from a normal disc of a patient"));

culturing said intervertebral disc cells under conditions to propagate disc tissue (page 2, lines 25-27 ("cultured in vitro in the presence of a cell stimulant ... to form monolayer cultures"), page 5, line 22-page 6, line 8; page 6, lines 10-29; page 6, lines 10-19 (materials may include collagen)); and

keeping said cultured disc tissue viable until use (page 10, lines 24-28 ("The cell density in the implantation carrier should be selected such that the cells will be capable of surviving, growing, and differentiating to form a healthy tissue.")).

Claim 54 is directed to mincing the tissue. Support may be found at page 2, lines 29-30 ("an explant is first obtained from a human disc specimen"); page 5, line 16 ("The disc tissue to be cultured is minced into 1-2 mm square pieces . . .".).

Claims 55-56 require that the explant be cultured in the presence of serum, growth factors or cytokines and on such growth factors as transforming growth factor beta (TGF-ß). Support may be found at page 3, lines 4-8 ("Typically, cell culture media, and optionally, cell stimulants such as fetal bovine serum, growth factors and the like are added to the three-dimensional structure such that the cells further proliferate and re-express extracellular matrix materials."); page 5, lines 26-31.

Claims 57-58 require that the cultured intervertebral disc tissue be combined with a carrier material such as one selected from alginate, agarose, collagen, and derivatives and mixtures there of. Support may be found at page 3, lines 2-4; page 6, line 10-page 8, line 3; page 8, line 26-page 9, line 16. In addition, collagen is specifically used in Example III (page 14.)

REQUEST THAT AN INTERFERENCE BE DECLARED

Pursuant to 35 U.S.C. §135 and 37 CFR § 1.607, Applicants respectfully request that an interference be declared between the above-identified application and United States Patent No. 6,340,369 to Bret A. Ferree.

IDENTIFICATION OF THE PATENT WHICH INCLUDES SUBJECT MATTER THAT INTERFERES WITH THE APPLICATION

United States Patent No. 6,340,369 to Ferree for "Treating Degenerative Disc Disease With Harvested Disc Cells and Analogues of the Extracellular Matrix" ("the Ferree patent") claims subject matter that interferes with the subject matter claimed in the present application ("the Hanley et al. application"). The Ferree patent (a copy of which is attached as Exhibit 1) issued on January 22, 2002 from Application No. 09/638,726, filed August 14, 2000 allegedly based upon a provisional Application No. 60/148,913, filed on August 13, 1999.

THE FERREE PATENT AND THE HANLEY ET AL. APPLICATION CLAIM INTERFERING SUBJECT MATTER

An interference is appropriate between an application and an unexpired patent of different parties when the application and the patent contain claims to the same patentable invention(s). 37 CFR § 1.601(i). 37 CFR § 1.601(n) provides a test for determining whether two parties claim the same patentable invention:

> Invention "A" is the "same patentable invention" as invention "B" when invention "A" is the same as [35 U.S.C. § 102] or obvious [35 U.S.C. § 103] in view of invention "B" assuming invention "B" is prior art with respect to "A".

As is apparent from this test, claims in an application or patent, are directed to the same invention as claims of another application or patent then the claims are patentably indistinct from each other. Here, Applicants' claims and the claims in the Ferree patent are patentably indistinct from each other. Thus, interfering subject matter is present.

The Ferree patent claims, *e.g.*, a method of treating a diseased or traumatized invertebral disc comprising the steps of harvesting live intervertebral disc cells; producing an engineered disc tissue; and transplanting the engineered disc tissue into the disc. The Hanley *et al.* application claims a method of treating an intervertebral disc disease or injury comprising the steps of obtaining live intervertebral disc tissue; culturing the tissue; implanting the cultured intervertebral disc cells into a target disc area. The Applicants' method of treating disc diseases

defines substantially the same method as Ferree's Claim 1. Similarly, because they recite methods of treatment of diseases by administering patentable indistinct compositions, Ferree's method Claim 1 is claiming the same invention as, for example, Hanley *et al.*'s Claim 39.

Secondly, the Ferree patent claims, *e.g.*, a method of preparing engineered invertebral disc tissue. The method comprises the steps of harvesting live intervertebral disc cells; producing an engineered disc tissue; and keeping the engineered disc tissue alive. The Hanley *et al.* application also claims a method of preparing invertebral disc tissue. The method comprising the steps of obtaining healthy intervertebral disc tissue; culturing the disc tissue and keeping the cultured disc tissue alive. The Applicants' method of preparing intervertebral disc tissue is substantially the same method as Ferree's Claim 20. Similarly, because they recite substantially identical methods for producing cultured disc tissue, Ferree's method of making a disc tissue Claim 20 is claiming the same invention as, for example, Hanley *et al.*'s Claim 52.

Thirdly, the Ferree patent claims, *e.g.*, a disc tissue made by harvesting live intervertebral disc cells; producing an engineered disc tissue; and keeping the engineered disc tissue alive. The Hanley *et al.* application also claims a disc tissue to be used in the method of treating disc diseases or injuries made by obtaining healthy intervertebral disc tissue; culturing the disc tissue and keeping the cultured disc tissue alive. The Applicants' disc tissue is substantially the same as Ferree's Claim 21. Similarly, because they recite substantially identical methods for producing cultured disc tissue, Ferree's product Claim 21 is claiming the same invention as, for example, Hanley *et al.*'s Claim 53.

Because there is no patentable distinction between the subject matter claimed by Ferree and that claimed by Applicants, the parties are claiming the same invention. *37 CFR § 1.601(n).* Accordingly, interfering subject matter is present even though the claims in the Ferree are not identical to those of applicants.

THE PROPOSED INTERFERENCE SHOULD HAVE THREE COUNTS

In formulating counts, the Examiner must decide both (1) how many counts there should be and (2) the scope of the counts. *M.P.E.P. § 2306.* In the sections that follow, Applicants present counts drafted to corresponding scope to the broadest of each party.

Each party (*i.e.*, Ferree and Hanley *et al.*) claims methods of treating intervertebral disc diseases or injuries, methods for making disc tissue and disc tissue made by the method of making claims. When separately patentable inventions are claimed by both parties, counts drawn to each separately patentable invention are required. *M.P.E.P. § 2306.* Accordingly, separate counts directed to methods of treating invertebral disc disease or injury, methods of making disc tissue and the disc tissue product are proposed.

FORMAT OF THE PROPOSED COUNTS

The parties' claims are not written in exactly the same manner. In proposing counts for this interference, Applicants have followed the widely-used convention of linking the two broadest corresponding claims from the present application and the Ferree patent by "OR." This proposal appears fair to both Ferree and Hanley *et al.*, and should simplify comparison of the claims of the parties to the counts as well as, for example, showing support for the counts in the specification of the parties.

Moreover, the proposed counts satisfy the requirements of 37 CFR § 1.606 that at the time an interference is initially declared, a count shall not be narrower in scope than any application claim that is patentable over the prior art and designated to correspond to the count, or any patent claim which corresponds to the count.

PRESENTATION OF PROPOSED COUNT I

Attached Appendix A sets forth alternatives for a Proposed Count I. Proposed Count I relates to a method for treating a diseased or injured intervertebral disc having nucleus and annulus regions comprising the steps of: (1) harvesting or (2) obtaining live intervertebral disc cells; (1) combining or (2) culturing the disc cells to produce an (1) engineered or (2) cultured disc tissue; and (1) transplanting or (2) implanting the (1) engineered or (2) cultured disc tissue into the disc of the patient. The Proposed Count I was prepared after consideration of the subject matter claimed by the respective parties. The count is being proposed in part because of the different language used by the respective parties to describe the same invention. Proposed Count I is at least as broad as Claim 1 of the Ferree patent.

Identification of Claims of the Ferree Patent Which Correspond to Proposed Count I

Claims 1, 4-10 of the Ferree patent correspond to Proposed Count I. Claim 1 of Ferree is substantially identical to the Proposed Count I before the word "OR", and thus must correspond to the proposed count. Claims 2-3 of Ferree are dependent from Claim 1, and, thus, must also correspond to Proposed Count I. Claim 12 also corresponds to Proposed Count I. Claim 12 claims a method of treating a diseased or traumatized intervertebral disc, comprising the steps of harvesting live cells from a human; adding therapeutic substances to the cells; transplanting the harvested cells into the disc being treated. Claims 13-19 depend from Claim 12 and, thus must also correspond to Proposed Count I.

Claims of the Hanley et al. Application Which Correspond to Proposed Count I

Claims 39-51 of the Hanley *et al.* application correspond to Proposed Count I. New Claim 39 is similar to Claim 20 originally filed in the parent application and is identical to the portion of Proposed Count I following "OR" and thus falls within, and must correspond to, the count. Claims 40-51 depend from Claim 39 and recite aspects of obtaining tissue, culturing tissue and implanting tissue. Thus, these claims fall within Claim 39, and correspond to Proposed Count I.

All claims identified as corresponding to Proposed Count I have either previously been in the present application or its parent application, and/or support for all the claims has been shown. *See pages 5-7 above.* Thus, the requirements of 37 CFR § 1.607(a)(5) are satisfied.

PRESENTATION OF A PROPOSED COUNT II

Also attached as part of Appendix A are alternatives for is a Proposed Count II. Proposed Count II is directed to a method of preparing intervertebral disc tissue comprising the steps of: (1) harvesting or (2) obtaining live intervertebral disc cells; (1) combining or (2) culturing the disc cells to produce a disc tissue; and keeping the disc tissue viable until use. The count is being proposed in this manner in part because of the different language used by the respective parties to describe the same invention. The Proposed Count II is at least as broad as Claim 20 of the Ferree patent.

Identification of Claims of the Ferree Patent Which Correspond to Proposed Count II

Claim 20 of the Ferree patent corresponds to Proposed Count II. Claim 20 of Ferree is substantially identical to the Proposed Count II before the word "OR", and thus must correspond to the Proposed Count II. Claim 32 also corresponds to proposed Count II. Claim 32 claims a method of preparing engineered intervertebral disc tissue comprising the steps of: harvesting or live intervertebral disc cells; combining the harvested disc cells to produce an engineered disc tissue; and transplanting while keeping the engineered disc tissue viable. Claim 35 depends from Claim 32 and, thus must also correspond to Proposed Count II.

Claims of the Hanley et al. Application Which Correspond to Proposed Count II

Claim 52 of the Hanley *et al.* application corresponds to Proposed Count II. New Claim 52 is identical to the portion of Proposed Count II following "OR" and thus falls within, and must correspond to, the count. Support for new Claim 52 corresponding to Proposed Count II has been shown. *See pages 5-7 above.* Thus, the requirements of 37 CFR § 1.607(a)(5) are satisfied.

PRESENTATION OF A PROPOSED COUNT III

Attached Appendix A sets forth alternatives for a Proposed Count III. Proposed Count III is directed to cultured disc tissue for use in treating human disc diseases or injuries prepared according to the steps of (1) harvesting or (2) obtaining live intervertebral disc cells; (1) combining or (2) culturing the disc cells to produce a disc tissue; and keeping the disc tissue viable until use. The Propose Count III is at least as broad as Claim 21 of the Ferree patent.

Identification of Claims of the Ferree Patent Which Correspond to Proposed Count III

Claim 21 of the Ferree patent corresponds to Proposed Count III. Claim 21 of Ferree is substantially identical to the Proposed Count III before the word "OR", and thus must correspond to the proposed count. Claim 21 is a product-by-process claims of Claim 20. Claims 22-27 of Ferree are dependent from Claim 21, and, thus, must also correspond to Proposed Count III. Claim 33 also corresponds to Proposed Count III. Claim 33 is a product-by-process claim depending from Claim 32. Claim 34 depends from Claim 33 and, thus must also correspond to proposed Count III.

Claims of the Hanley et al. Application Which Correspond to Proposed Count III

Claims 53-58 of the Hanley *et al.* application correspond to Proposed Count III. New Claim 53 is identical to the portion of Proposed Count III following "OR" and thus falls within, and must correspond to, the count. Claims 54-58 depend from Claim 53 and recite aspects of obtaining tissue, culturing tissue and implanting tissue. Thus, these claims fall within Claim 53, and correspond to Proposed Count III.

Support for new Claims 53-58 corresponding to Proposed Count III have either previously been in the application and/or support for all the claims has been shown. *See pages 5-7 above.* Thus, the requirements of 37 CFR § 1.607(a)(5) are satisfied.

THE REQUIREMENTS OF 35 U.S.C. § 135(b) ARE SATISFIED

The Ferree patent issued on January 22, 2002. Therefore, the requirements of 35 U.S.C. § 135(b) are satisfied if Hanley *et al.* have presented the claims for the same or substantially the same subject matter as the claims in the Ferree patent prior to January 22, 2003. That there is no issue of compliance with this requirement can be seen by comparing Hanley *et al.* Claim 39, to the method of treating disc disease or injury, presented in the originally filed parent application (Claim 13) filed November 26, 1997 and in the present application (Claim 20) filed April 27, 2000 with Ferree Claim 1.

HANLEY et al. SHOULD BE DESIGNATED AS SENIOR PARTY

The present Hanley *et al.* application is a continuation-in-part application of application Ser. No. 08/979,674 filed November 26, 1997, now United States Patent No. 6,080,579. As shown below, Hanley *et al.* should be accorded benefit of this prior application in the declaration of interference of all counts. Hanley *et al.* should also be designated as senior party in the interference as having the earlier effective filing date, *i.e.*, November 26, 1997, versus allegedly August 13, 1999 for the Ferree patent.

With respect to proposed Count I, support is found in the parent application Ser. No. 08/979,674* as follows:

"A method of treating a diseased or injured invertebral disc: page 4, lines 1-4; page 6, lines 20-24; claims 13 and 26.

having nucleus and annulus regions: page 6, lines 29-31; page 10, lines 10-12

obtaining live intervertebral disc cells: page 2, lines 8-9;

culturing said intervertebral disc cells under conditions to propagate disc tissue: page 4, lines 7-22; page 5, lines 1-16; page 7, line 11-page 9, line 18; page 16, lines 4-7 (production of extracellular matrix components; Example III use of collagen;

implanting the cultured disc tissue into a target disc area needing treatment in a human patient: page 2, lines 22-25; page 5, lines 28-30; page 6, lines 16-17.

Because support for Proposed Count I is in the parent application, Hanley *et al.* should be given benefit of the filing date of November 26, 1997 of application Ser. No. 08/979,674 with respect to Count I, and be named senior party. In addition, the Applicants have shown support for all of the claim limitation in the instant application, see pages 5-7 supra, the Applicants should be named senior party by virtue of the filing date of the instant application of April 27, 2000 should Ferree's provisional application fail to support the Count.

With respect to proposed Count II, support is found in the parent Application No. 08/979,674 as follows:

Claim 52 is directed to a method for preparing a cultured intervertebral disc tissue comprising; obtaining live intervertebral disc tissue; culturing the disc tissue; and keeping the cultured disc tissue viable until use. Support for Claim 52 may be found as follows:

obtaining live intervertebral disc cells: page 2, lines 8-9;

culturing said intervertebral disc cells under conditions to propagate disc tissue: page 4, lines 7-22 ; page 5, line 1-16; page 7, line 11-page 9, line 18; page 16, lines 4-7 (production of extracellular matrix components; and Example III use of collagen); and

* A copy of the specification of Ser. No. 08/979,674 is attached as Exhibit 2. Reference to page and line number are to the copy of the specification presented in Exhibit 2. It should also be noted that support is found in the present application filed April 27, 2000. *See pages 5-7, supra.*

keeping said cultured disc tissue viable until use (page 10, lines 24-28)("The cell density in the implantation carrier should be selected such that the cells will be capable of surviving, growing, and differentiating to form a healthy tissue.").

Because support for Proposed Count II is in the parent application, Hanley *et al.* should be given benefit of application No. 08/979,674 with respect to Count II, and be named senior party.

With respect to proposed Count III, support is found in the parent Application No. 08/979,674 as follows:

Claim 53 is directed to the disc tissue made by the steps of preparing a cultured intervertebral disc tissue comprising; obtaining live intervertebral disc tissue; culturing the disc tissue; and keeping the cultured disc tissue viable until use. Support for Claim 53 may be found as follows:

obtaining live intervertebral disc cells: page 2,lines 8-9;

culturing said intervertebral disc cells under conditions to propagate disc tissue: page 4, lines 7-22 ; page 5, line 1-16; page 7, line 11-page 9, line 18; page 16, lines 4-7 (production of extracellular matrix components; and Example III use of collagen); and

keeping said cultured disc tissue viable until use (page 10, lines 24-28)("The cell density in the implantation carrier should be selected such that the cells will be capable of surviving, growing, and differentiating to form a healthy tissue.").

Because support for Proposed Count III is in the parent application, Hanley *et al.* should be given benefit of application No. 08/979,674 with respect to Count III, and be named senior party.

CONCLUSION

An interference between the Ferree patent and the present application is appropriate. The interference should be declared employing the Proposed Count I as set forth on attached Appendix A with Claims 1-10 and 12-19 of the Ferree patent, and Claims 39-51 of the instant application being designated as corresponding to Count I. The interference should also include a second count, Proposed Count II set forth and attached as Appendix A. Claims 20, 32 and 35 of the Ferree patent and Claim 52 of the instant application should be designated as corresponding

to proposed Count II. The interference should also include a second count, Proposed Count III set forth and attached as Appendix A. Claims 21 and 33-34 of the Ferree patent and Claims 53-58 of the instant application should be designated as corresponding to proposed Count III.

In the declaration of interference, the present application should be accorded benefit of parent application No. 08/979,674, filed November 26, 1997, and the Hanley *et al.*, should be designated as senior party.

Claims 35-38 of the Hanley et al. application are directed to therapeutic composition for treating human disc diseases comprising a carrier in admixture with *in vitro* propagated human intervertebral disc cells being prepared by a series of steps forming a three-dimensional structure. These claims do not interference with any claims in the Ferree patent. Therefore these claims should not be designated as corresponding to any of the counts.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

Ernest B. Lipscomb III

Ernest B. Lipscomb, III
Registration No. 24,733

Customer No. 00826
ALSTON & BIRD LLP
Bank of America Plaza
101 South Tryon Street, Suite 4000
Charlotte, NC 28280-4000
Tel Charlotte Office (704) 444-1000
Fax Charlotte Office (704) 444-1111

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, Washington, DC 20231, on May 30, 2002.

Janet F. Moore

APPENDIX A

PROPOSED COUNT I

A method of treating a diseased or traumatized invertebral disc having a nucleus and annulus fibrosis, comprising the steps of:

harvesting live intervertebral disc cells;

combining the harvested cells with an analogue of the extracellular matrix to produce an engineered disc tissue; and

transplanting the engineered disc tissue into the disc.

OR

A method of treating a diseased or injured invertebral disc having nucleus and annulus regions, comprising the steps of:

obtaining live intervertebral disc cells;

culturing said intervertebral disc cells under conditions to propagate disc tissue; and

implanting said cultured disc tissue into a target area needing treatment in a human patient.

PROPOSED COUNT II

A method of preparing engineered intervertebral disc tissue, comprising the steps of:

harvesting live intervertebral disc cells;

combining the harvested cells with an analogue of the extracellular matrix to produce an engineered disc tissue; and

keeping the engineered disc tissue viable until use.

OR

A method of preparing cultured intervertebral disc tissue, comprising the steps of:

obtaining live intervertebral disc cells;

culturing said intervertebral disc cells under conditions to propagate disc tissue; and; and

keeping the cultured disc tissue viable until use.

PROPOSED COUNT III

A engineered disc tissue prepared according to the steps of:

harvesting live intervertebral disc cells;

combining the harvested cells with an analogue of the extracellular matrix to produce a cultured disc tissue; and

keeping said cultured disc tissue viable until use.

OR

A cultured disc tissue for use in treating human disc diseases prepared according to the steps of:

obtaining live intervertebral disc cells;

culturing said live intervertebral disc cells under conditions to propagate disc tissue; and;

keeping the cultured disc tissue viable until use.